Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Conclusion: Results from this IA provide the earliest evidence from multicenter real-world settings demonstrating clinically meaningful improvements with elexacaftor/tezacaftor/ivacaftor and ivacaftor in lung function, nutritional status, and PEx rate among PwCF, consistent with findings from pivotal clinical trials.
Acknowledgements: Sponsor: Vertex Pharmaceuticals Incorporated.

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Secular drift in predictive accuracy of pulmonary exacerbations: A registry study

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Background: Predicting the onset of pulmonary exacerbation (PE) for people with cystic fibrosis (CF) is critical as it identifies those at high risk in advance and allows timely clinical intervention. Data patterns are changing over time, especially with the introduction of ivacaftor treatment in 2012 followed by other highly effective modulator therapies (HEMTs). The epidemiologic impact of secular trends in CF care and treatments on PE prediction has not been studied.
Methods: We evaluated prediction model "drift" using a longitudinal retrospective cohort of 29,476 individuals from the CF Foundation Patient Registry (CFF-PR) over 2011–2018 and applying a Gaussian linear mixed effects model with random intercept and integrated Brownian motion to account for between-subject variation and changes within a given subject over time. Each PE event was defined using the CF Foundation's definition known as FEV1-indicated exacerbation signal (FIES), which is based on relative drops in FEV1% predicted. We formed predictive probabilities for each FIES event using a target function based on the model. Demographic and clinical characteristics established as predictors of FEV1 decline were included as covariates. To account for HEMT introduction, we considered a treatment model that included ivacaftor use as a covariate. Models were trained using 2-year window data cuts including data from 2011 onward. Prediction performance of each of the 6 models was tested on the subsequent years.
Results: In testing subsequent years with models from the prior windows, AUC reductions ranged from –0.32% to 3.28% (see Drop% by Row in Table 1). Using the 2011–2012 model to fit 2015 lung function data resulted in a significant drop of 1.03%. When testing remaining models, the AUC drop rates of the subsequent years were all below 1.07%, though some drops were significant. Among all the models, the greatest drop was 3.28% when comparing 2018's AUC (0.7757) against 2013's (0.8015) in the 2011–2012 model. We also compared the models fitted to the data for the previous years to later years and the percent of drop ranged from 0.04% to 3.7% (see Drop% by Column in Table 1). Although the models including ivacaftor use have similar accuracy across windows as those excluding ivacaftor as a covariate, its inclusion significantly improved model fit (likelihood ratio test, $P < 0.001$).

		2013	2014	2015	2016	2017	2018
2011-2012	AUC	0.8015	0.7968	0.7933	0.7889	0.7873	0.7757
	Drop% by Row		0.59%	1.03%	1.59%	1.8%	3.28%
	Drop% by Column		1.65%	2.12%	2.6%	3.27%	3.7%
2012-2013	AUC		0.8102	0.8097	0.8083	0.8104	0.8017
	Drop% by Row			0.06%	0.23%	-0.02%	1.05%
	Drop% by Column			0.1%	0.21%	0.43%	0.47%
2013-2014	AUC			0.8105	0.8094	0.8117	0.8031
	Drop% by Row				0.14%	-0.15%	0.91%
	Drop% by Column				0.07%	0.27%	0.3%
2014-2015	AUC				0.81	0.8126	0.8039
	Drop% by Row					-0.32%	0.75%
	Drop% by Column					0.16%	0.2%
2015-2016	AUC					0.8139	0.8052
	Drop% by Row						1.07%
	Drop% by Column						0.04%
2016-2017	AUC						0.8055

Table 1. Treatment model performance evaluated by area under the receiver operating characteristic curve (AUC).Rows are grouped by the training data and columns indicate the years of test data. Drop %s are compared to the diagonal elements highlighted in gray.

Conclusion: While model fit improved accounting for ivacaftor, prediction performance was similar. The most impactful model drift occurred after 2012 coinciding with increased HEMT use.

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Seroprevalence of COVID-19 IgG in the cystic fibrosis population

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Background: Since the first known U.S. case of COVID-19 was reported in early 2020, little was known about the prevalence in the cystic fibrosis (CF) population. CF is a genetic disorder caused by more than 1,700 different mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene resulting in a wide spectrum of disease phenotypes. As the majority of individuals with CF have chronic lung disease, this population is considered to be high risk for severe disease if infected with any virus, especially that of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). As the number of cases in the United States nears 31 million and the number of deaths in the United States is currently reported at greater than 560,000, the prevalence of COVID-19 in the CF population remains largely unknown, although the clinical course for those infected is becoming more clear. To date, the Cystic Fibrosis Foundation reported 1,383 cases of COVID-19 in the United States and 14 people who have died, giving a case fatality rate of 1.0%.
Methods: Early in the course of the pandemic, we began studying the exposures and symptoms of people with CF to evaluate the prevalence of COVID-19 IgG antibody in patients who receive care at the MN CF Center. Individuals >/ = 12 years of age completed a brief, online survey detailing possible exposures, symptoms of COVID-19, and behavioral data (e.g., social distancing practices). We extracted additional data through the electronic medical record (EMR) to identify risk factors for COVID-19 IgG development including age, BMI, sex, FEV1 (forced expiratory volume in 1 second), CFTR modulator use, and diabetes. Participants were evaluated for COVID-19 IgG at the time of enrollment (0 months) and the natural history of COVID-19 IgG will be further elucidated with additional Ab testing at 6 months and 12 months post-enrollment.
Results: Early data includes 115 enrollees with an average age of 35 years. 49.6% of participants are female. Of those tested, 9.6% had a positive COVID IgG test. Of those who tested positive, the < 30 year old age group had the highest rate of seropositivity at 63.6%. At this time, 7.8% of the enrolled participants have been vaccinated against SARS-CoV-2.
Conclusion: SARS-CoV-2 is becoming more prevalent in the state of Minnesota, and the prevalence of COVID-19 IgG in individuals with cystic fibrosis suggests similar exposure as the general community. Additional

data collection at 6 months and 12 months will identify the natural progression of IgG in CF patients in response to COVID-19.

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The essential role of the community health worker in rural CF clinics

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Background: The University of Texas Health Science Center at Tyler (UTHSCT) serves Northeast Texas, a 35-county region with a population close to 1.5 million with more than half in rural areas. When compared to urban residents, rural residents experience more challenges in health care due to financial constraints, scarcity of services, insufficient transportation, and poor internet service [1]. Consequently, they are generally in poorer health with unmet health navigation needs and health literacy limitations [2]. Our CF clinic encounters the same challenges, as many patients seek help with health care navigation tasks, including insurance sign up and Trikafta paperwork. Our patients express that the processes to obtain resources are complex and difficult. Community health workers (CHW) improve health care by providing patients with health knowledge, promoting self-sufficiency, and increasing access to health care through education, advocacy, as well as social support [3]. In 2016, the CF foundation provided funding for a mental health coordinator for our clinic for 3 years. Upon conclusion of the grant, limited support was provided by social workers or the psychology department. Such services were not adequately addressing patient needs, and UTHSCT responded by providing funding for a CHW. Prior to February 2021, our clinic did not systemically document resource assistance. The purpose of this study is to quantify the valuable role of the CHW by tracking patient health access increase with CHW assistance.

Methods: In February 2021, a database was created through an Excel spreadsheet to record the number of patients helped, types of resources requested, number of resources attained, time spent in direct patient contact, and resource attainment success rates. Data collection will remain in progress.

Results: Data collected from February 8, 2021, to April 7, 2021, indicate our CHW assisted close to 40 patients and spent approximately 18 hours in direct patient contact; there were 40 successful attempts in connecting patients with resources. The resources include the COVID vaccine, modulators, and insurance. More detailed analysis, including the reasons for unsuccessful attempts of resource attainment, will be presented.

Conclusion: The preliminary data suggests a lot of time and many patient contacts are needed to increase patient access to resources. By identifying the success rates, types of resources sought by patients, as well as time needed to gain access, CF clinics can advocate for expansion of resources, dedicate sufficient time for health care navigation, and identify more beneficial resources to patients in order to improve their health.

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The real-world effectiveness of U.S. CF newborn screening

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Background: Implementation of universal newborn screening (NBS) for cystic fibrosis (CF) was achieved in the United States in 2010. The Wisconsin randomized controlled trial of NBS demonstrated early and sustained improvements in growth, but no clear pulmonary benefits of NBS. Evaluating NBS in the current era is necessary, as the Wisconsin trial evaluated outcomes prior to recent advances in CF care regarding nutrition, infection control, *Pseudomonas aeruginosa* eradication protocols, and chronic therapies. Our objective was to estimate the effect of CF NBS on longitudinal health outcomes a decade after universal implementation in the United States. We hypothesized that, compared to infants diagnosed prior to the introduction of NBS in their state of birth, infants diagnosed after NBS was implemented would achieve better outcomes in growth, pulmonary function, and age at *P. aeruginosa* infection.

Methods: We conducted a stepped-wedge cohort study utilizing 2018 U.S. CF Foundation Patient Registry to estimate the effect of NBS, accounting for the staggered implementation of NBS from 2000 through 2009 across 44 states. Children with a diagnosis of CF, born 2000 or later in these states, were included and categorized by NBS status (born prior to or following initiation of NBS in state of birth). Separate linear mixed effects models with an interaction between NBS status and age were used to estimate the effect of NBS on FEV1% predicted, weight and height percentiles. Cox proportional hazards models were used to estimate the effect of NBS on age at initial and chronic *P. aeruginosa*. All models estimated outcomes through age 9 years; were adjusted for birth cohort, sex, CFTR genotype and insurance status; and accounted for state-level random effects.

Results: The cohort included 4,624 children born before and 5,075 children born after NBS implementation in their state of birth. Comparing the pre- to post-NBS cohorts, mean age at diagnosis was 17.2 (95% CI 16.3–18.1) versus 2.1 (95% CI 1.8–2.4) months. The post-NBS cohort had a higher percentage that attained height and weight ≥50th percentile compared to pre-NBS at age 3 years (height 51.8% vs 41.2%, weight 63.8% vs 52.6%) and 6 years (height 45.6% vs 36.4%, weight 58.0% vs 48.2%). The hazard of initial *P. aeruginosa* was 18% lower (HR: 0.82, 95% CI, 0.72–0.94) and chronic *P. aeruginosa* 34% lower (HR 0.66, 95% CI, 0.48–0.89) in the post-NBS cohort compared to the pre-NBS cohort. At 9 years, estimated mean FEV1% predicted in pre- and post-NBS cohorts was 98.6 (95% CI, 96.2–100.9) versus 100.9 (95% CI, 99.4–102.3), with evidence that the effect of NBS varied by age. Complete modeling results for all outcomes will be presented.

Conclusion: We demonstrate that CF NBS in the United States is associated with improved outcomes through age 9 in a "real-world" setting using a novel stepped-wedge cohort study design to account for improving CF outcomes over time. Children diagnosed following the introduction of NBS in their state were more likely to achieve nutritional goals and had lower hazard of initial and chronic *P. aeruginosa* infection than children born prior to NBS. Estimated mean lung function by age 9 was 2% higher in the post-NBS group, though this difference was not statistically significant. Continued follow-up will evaluate whether childhood outcomes associated with NBS translate to improved long-term outcomes.